

REMARKS

Status of the Claims

After entry of the instant amendment, claims 1-5 and 8-17 are pending. Claims 1 and 16 are independent.

Claims 6 and 7 have been cancelled and claims 1, 2, 4, 5, 9, 10, 12-14 and 16 have been amended without prejudice or disclaimer of the subject matter contained therein. New claim 17 has been added. Applicants have amended the claims in order to correct minor errors and to place the claims in better form. The claims have been amended to recite the subject matter therein more clearly.

Support for amendments made to claims 1, 2, 4, 5, 9, 10, 12-14 and 16 can at least be found in original claims 6, 7 and 10; at page 6, lines 5-11; at page 6, line 33 to page 7, line 2; at page 7, lines 13-21; at page 8, lines 12-16; at page 9, line 35 to page 10, line 5; at page 10, line 36 to page 11, line 5; at page 11, lines 30-36; at page 12, lines 31-37; and at page 13, lines 22-28 of the present Specification. Support for new claim 17 can at least be found at page 8, lines 6-10 and the Examples of the present Specification. Thus, no new matter has been added by way of the amendments made to the claims.

Reconsideration of this application, as amended, is respectfully requested.

Request for Entry of Response After Final Rejection

In the event that this response does not place this application in condition for allowance, the Examiner is requested to enter this response because it places the application in better condition for appeal.

Obviousness-Type Double Patenting Rejection

Claims 1-10 and 12-14 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting over copending Application No. 10/594,740 (hereinafter the "'740 Application'") and Application No. 10/492,346 (now granted as US Patent No. 7,390,411). It is respectfully requested that the double patenting rejection over the '740 Application be withdrawn at least until one of the involved applications grants a patent, especially since the scope of the claims will likely change so as to affect double patenting issues. Regarding the double patenting rejection over the '411 Patent, it is submitted that the patentable distinctions

over the cited Freiss et al. reference (WO 03/030867) discussed below also apply to the distinctions between the claims of the present application and the claims of the U.S. Patent No. 7,390,411, those distinctions being deemed repeated herein. Thus, this double patenting rejection should also be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 16 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, it is asserted that the phrase “wherein step (a) is conducted in the absence of carbon dioxide,” recited in claim 16, is not clearly disclosed in the Specification, as filed. Applicants respectfully disagree with this assertion. However, in order to expedite prosecution of the present application, Applicants have deleted the phrase from claim 16.

In view of the amendment of claim 16, Applicants respectfully request that the rejection of claim 16 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejections under 35 U.S.C. §§ 102(b) and 103(a)

Claims 1-8, 10, 12 and 13 stand rejected under 35 U.S.C. § 102(b) as being anticipated by the English translation of Freiss et al., WO 03/030867 (hereinafter “Freiss”). This rejection is respectfully traversed.

Claims 1-10, 12-14 and 16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Freiss in view of Chowdhary et al., U.S. Patent No. 6,693,093 (hereinafter “Chowdhary”).

At page 9, line 19 to page 10, line 2, of the Freiss reference, Freiss distinguishes his invention over that of the prior art, stating:

The inventors of the present application have discovered, surprisingly, that a method comprising the steps of generating an anilide derivative by a supercritical fluid, mixing it with a porous support, followed by a step of molecular diffusion by the supercritical fluid in static mode and of washing with the supercritical fluid, makes it possible to prepare an interaction compound by very greatly increasing the solubility of the anilide derivative in an aqueous medium, and hence its bioavailability...washing in a supercritical medium, which consists in eliminating the residual solvents by passage of a flow of supercritical CO₂, also makes it possible, surprisingly, besides the washing of the interaction compound, to increase the dissolution following this step. [emphasis added]

Thus, Freiss teaches a required wash step using supercritical fluid and that this wash step is responsible, at least in part, for the improved solubility of the anilide derivative, making it more bioavailable. The claimed invention consists of (a) mixing active substances with host molecules and water, (b) carrying out a molecular diffusion step by bringing supercritical fluid into contact with the mixture, and (c) recovering the molecular complex that is formed. Thus, the claimed invention does not include the washing step that Freiss has taught is essential in producing a complex that causes an anilide derivative to be more soluble in water.

Furthermore, Freiss teaches methods requiring an “anilide derivative generated by a supercritical fluid” (claim 1; page 9, lines 19-28; page 11, lines 26-34; page 12, line 32 to page 15, line 14; and the Examples). Such processing causes the anilide derivative to have a greater specific surface area and can enhance its solubility (page 11, lines 26-33). In order to produce Freiss’ “anilide derivative generated by supercritical fluid,” (a) the anilide derivative is first dissolved in a supercritical fluid (optionally, admixed with a co-solvent, like DMSO) or in an organic solvent or (b) both the anilide derivative and a porous support are first dissolved in an organic solvent before being contacted with a supercritical fluid (page 12, line 32 to page 15, line 14; and the Examples).

For example, at page 12, line 35 to page 13, line 2 of Freiss, the active substance (an anilide derivative) and the porous support (*i.e.*, the cyclodextrin) are brought into contact with one another using an organic solvent. The anilide derivative and the cyclodextrin are dissolved by the organic solvent and the organic solvent is also soluble in the supercritical fluid that is subsequently brought into contact with the solution.

The active substances of the claimed methods of the present application are not first dissolved in an organic solvent or supercritical fluid (optionally admixed with a co-solvent), as taught by Freiss. In the claimed methods, active substances are mixed with host molecule components and water, and, as the active substances are only poorly soluble in the water, active substances are only slightly dissolved in the water, if at all. The pending claims do not include an organic solvent that is used to dissolve the active substances.

Therefore, the claimed methods differ from those taught by Freiss in that the active substance (*e.g.*, anilide derivative) is first mixed with water (in which it does not dissolve or only slightly dissolves) before being brought into contact with a supercritical fluid, and not first dissolved with a supercritical fluid or with an organic solvent, as taught by Freiss.

As explained above, Freiss teaches methods that require both a washing step with supercritical fluid after step (b) and a step of generating an active substance using a supercritical fluid before step (a). The claimed methods do not comprising a washing step as taught by Freiss, and the active substances recited in the claimed methods do not have to be generated using a supercritical fluid, as Freiss teaches is essential to his invention. In view of the teachings of Freiss, one of skill in the art would not expect that the claimed processes would be capable of producing complexes with enhanced aqueous solubility of the active substances without including a washing step and/or a step for generating the active substance using a supercritical fluid.

In the Office Action it is pointed out that at page 7, lines 6-25, Freiss teaches that methods are known in the prior art that use active substances, which are not generated by supercritical fluids and that do not employ a washing step with a supercritical fluid. However, Freiss distinguishes his invention over such prior art as he indicates that these two steps are essential (page 9, lines 19-28).

The inventors of the claimed invention have unexpectedly found that these two steps are, in fact, not necessary for obtaining good aqueous solubility of a molecular complex containing active substances produced by methods where the active substance and the host molecules are mixed with water prior to being contacted with a supercritical fluid. Applicants, therefore, respectfully point out that the claimed methods are new and novel (involving an inventive step) in view of the teachings of Freiss.

To reiterate, the claimed methods differ from those taught by Freiss in that the active substance is first mixed with water before being brought into contact with a supercritical fluid, and not first dissolved with a supercritical fluid or with an organic solvent, as taught by Freiss. Further, Freiss teaches that a washing step with supercritical fluid is essential, and the claimed invention does not include such a washing step. Likewise, Freiss' methods require an anilide derivative generated by a supercritical fluid to achieve enhanced solubility/bioavailability of the anilide derivative, and this is not a requirement of the claimed methods. Chowdhary does nothing to overcome the deficiencies of the teachings of Freiss.

In view of the discussion above, Applicants respectfully request that the rejections of claims 1-10, 12-14 and 16 under 35 U.S.C. §§ 102(b) and 103(a) be withdrawn.

New Claim 17

It is unexpected that step (b) need be carried out for only two hours in order to achieve molecular diffusion, as the prior art (*i.e.*, Freiss) indicates that molecular diffusion should require about 16 hours (page 16, line 7). Thus, Freiss does not teach or suggest the invention recited in claim 17.

CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Stephanie A. Wardwell, Ph.D., Registration No. 48,025 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: APR 14 2010

Respectfully submitted,

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